



Appl. No. : 09/901,121  
Applicant : Wei-Sing CHU  
Filed : July 10, 2001  
TC/A.U. : 1641  
Examiner : Nelson C. Yang

Confirmation No. 8944

Docket No. : 2313-0115  
Cust. No. : 06449

Commissioner for Patents  
P.O. Box 1450  
Alexandria VA 22313-1450

### AMENDMENT

Dear Sir:

In response to the Office action of October 6, 2003, please amend the subject application as follows:

Amendments to the Specification begin on page 2 of this paper.

Amendments to the claims are reflected in the listing of claims which begins on page 4 of this paper.

Remarks begin on page 7 of this paper.

An Appendix including a copy of a Petition to Accept Color Photographs filed July 10, 2001 follows page 10.

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Amendments to the Specification:

Please amend the specification of record as follows. No new matter has been added.

Please amend the paragraph at page 23, between lines 8 and 18, as follows:

The methods disclosed herein describe a novel technique for rapidly preserving tissues for morphologic, biochemical and molecular studies. The ultrasound-mediated fixation and processing method allow preservation of high quality morphology, proteins and mRNA from routine formalin fixation and processing. The technique is fast, simple, easy to perform, and versatile. The ultrasound fixed and processed tissue may be used for rapid IHC or ISH or for rapid clinical pathology diagnosis. High quality fixed tissue sections may be used for laser capture microdissection, mRNA extraction and PCR studies. Solid phases such as hHigh quality fixed tissue blocks may be used for high-throughput tissue microarray analyses of the DNA, RNA and protein targets for a large series of cancer research. The techniques described can be applied not only to tissue sections but also to assays being performed on a membrane (e.g., Northern, Southern and Westerns), on DNA chips, or on any other type of microarray.

Please amend the paragraph at page 8, between lines 22 and 28, as follows:

Figure 5B is a schematic of one possible setup for performing fixation and processing of a tissue sample while using ultrasound as part of the process. It is similar to the setup of Figure 5A but includes more aspects. The ultrasound generator puts out high frequency, high intensity waves which can be of a single frequency or a wideband frequency and can be continuous or pulsed. The transducer or transducers can have one head or multiple heads. Different intensities may be produced with different heads or with multiple transducers. The sample can be rotated or the transducers can revolve around the sample to aid in producing an even ultrasound field. This can be performed in one, two or three dimensions (1D, 2D and 3D).

Please amend the paragraph at page 17, between lines 18 and 30, as follows:

A more general ultrasound system setup is illustrated in Figure 5A. An ultrasound

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generator produces ultrasound which irradiates a sample. Sensors are present to measure the incident ultrasound intensity and can also measure ultrasound intensity which passes through the sample, size of the sample, temperature of the sample, etc. Data from the sensors feeds into a central processing unit which can control the ultrasound generator as well as control movement of samples into and out of a reaction chamber, change solution or solvent within a reaction chamber, etc. Preferably when this is used for fixation and processing of a tissue sample a high frequency  $> 0.1$  MHz and high intensity  $> 5$  W/cm<sup>2</sup> is used. An even field of ultrasound radiation is also preferred. Figure 5B represents further options including use of either a single frequency or a wideband of frequencies of ultrasound radiation. The radiation can be continuous or given in pulses. A frequency or an intensity of the pulses may be varied. Transducers can have one head or multiple heads. To produce a more even field of radiation on the tissue sample, the sample can be rotated and/or the ultrasound transducers can be revolved around the sample. Different intensities may be produced with different heads or with multiple transducers.